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Impact of effective platelet–rich plasma in treatment for knee osteoarthritis

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ABSTRACT

Background

Platelet-rich plasma (PRP) injections have become an intriguing treatment option for osteoarthritis (OA), particularly OA of the knee. There is a paucity of high-level evidence that is comparable, cohort specific, dose controlled injection protocol controlled and double-blinded.

Purpose

To assess the safety and efficacy of platelet-rich plasma (PRP) for knee OA treatment through feasibility trial regulated by the US Food and Drug Administration (FDA).

Study design

A prospective observational study.

Method

In accordance with FDA protocol, patient selection was based on strict inclusion/exclusion criteria; 30patients were screened and included in the study. These patients were received platelet-rich plasma (PRP).Western Ontario and McMaster universities osteoarthritis Index (WOMAC), Visual Analogue Scale (VAS) scores served as the primary efficacy outcome measures. Patients were followed for 3 months. The present study carried out in Gandhi Medical College and Hospital, Telangana, India to study the Impact of PRP in the treatment of knee osteoarthritis.

Results

No adverse events were reported for PRP administration. Furthermore, the results demonstrated no statistically significant difference in baseline WOMAC, VAS score. However; WOMAC scores at 1 week were significantly decreased compared with baseline scores, and the scores for this group remained significantly lower throughout the study duration. At the study conclusion (3 months), improved overall WOMAC scores by 80% from their baseline score.

Conclusion

PRP is safe and provides quantifiable benefits for pain relief and functional improvement with regard to knee Osteoarthritis. No adverse events were reported for PRP administration. After 3 months, WOMAC scores improved by 80% from their baseline score. Other joints affected with OA may also benefit from this treatment.

Keywords: FDA; Platelet-rich plasma (PRP); Osteoarthritis (OA); WOMAC and VAS pain scales.

INTRODUCTION

Osteoarthritis is typical productive, progressive arthropathy disorder primarily affecting weight bearing by diarthrodial joints of the peripheral and axial skeleton it is characterized by progressive deterioration and loss of articular cartilage, resulting in heberden's and bouchard's nodes are bony (0steophytes) formation, pain, limitations of motion, deformity and progressive disability. Inflammation may or may not be present in the affected joints. Osteoarthritis is considered as a result of excessive mechanical stress applied to susceptible joints predisposed on chondrocyte dysfunction (that may be genetic or environmental). Physical examination of affected joints reveals tenderness, crepitus and possible joint enlargement [1].

Platelet –rich plasma (PRP) is also known as platelet rich growth factors (GFs), Platelet rich fibrin (PRF) matrix, and platelet concentrate. Platelet rich plasma (PRP) also known as autologous conditioned plasma is a concentrate of platelet rich plasma protein derived from whole blood, centrifuged to remove red blood cells [2].

Composition includes whole blood placed in Centrifuge prior to two stage centrifugation There are four general categories of preparation of PRP based on its leukocyte and fibrin content leukocyte-rich PRP (L-PRP), leukocyte reduced PRP (P-PRP; leukocyte reduced or pure PRP), leukocyte platelet-rich fibrin and pure platelet-rich fibrin. The efficacy of certain growth factors in healing various injuries and the concentrations of these growth factors found within PRP are the theoretical basis for the use of PRP in tissue repair. The platelets collected in PRP are activated by the addition of thrombin and calcium chloride, which induces the release of the mentioned factors from alpha granules. The growth factors and other cytokines present in PRP include: platelet- derived growth factor, transforming growth factor beta, fibroblast growth factor, insulin-like growth factor 1, insulin-like growthfactor2, vascular endothelial growth factor, epidermal growth, interleukin 8, keratinocyte growth factor, connective tissue growth factor [3, 4].

Based on the various above literatures and their report we have decided to assess the use of PRP in treatment of knee osteoarthritis. Furthermore we want to explore the study and efficacy of the application of platelet rich plasma (PRP) in treatment of osteoarthritis and degenerative lesions of the articular cartilage of the knee and to check feasibility study to assess the safety intervention procedure and to assess primary and secondary outcome measures [5].

METHODS

FDA oversight

The study was performed under guidelines established by the FDA. For this trial, the main concept governing FDA approval was the safety and tolerability of PRP treatment in patients with OA who had failed non-operative treatment for at least 6 weeks. Safety was the primary outcome of this study. In addition, evaluation of clinical efficacy was performed as a secondary outcome to ensure reliability of physical function. To assess the potential therapeutic effects Western Ontario and McMaster universities Osteoarthritis Index (WOMAC) and visual analogue scale (VAS) scores is used. The FDA's review of the study was focused on the safety and efficacy of the PRP and whether the potential benefit of the PRP injection justifies the overall risk.

Study parameters

This was designed as a prospective, single center and double-blind (patient and investigator) study. Subject recruitment occurred through a clinical evaluation of patients seeking treatment for knee OA from the primary investigator. Patient selection is based on strict inclusion/exclusion

criteria (Table 1); 30 patients were screened, monitored by primary investigator to receive PRP injection. The study was designed to evaluate the safety and efficacy of PRP injection over 3-months period. Patients in treatment were allowed to take only diclofenac sodium for breakthrough pain.

Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index).All patients had a screening visit 1 and visit 2 at 1 week, visit 3 at 2 weeks, visit 3 at 3 weeks, visit 4 at 1 month followed by end-of-study visit 5 at 3 months. A reduction in WOMAC score is suggestive of improvement in the patient's condition.

Table-1 Subject eligibility criteria

Study Period: 6 months.
Sample: 30 patients.

Inclusion criteria

- Age between 30 to 60 years
- Adults both male and female
- The patients with early osteoarthritis(GRADE I and GRADE II)
- Patients without co morbidities
- WOMAC AND VAS pain scales

Exclusion criteria

- Age below 30 and above 60 years
- Pregnant women and lactating mothers
- Advanced osteoarthritis (GRADE III and GRADE IV)
- If patient is absconded
- If patient die
- Systemic or OA injection of corticosteroids in any joint within 3 months before screening
- Previous surgery at the target knee within the past 6 months
- History of infection or current infection at the affected joint

Procedure for the preparation of platelet rich plasma (PRP)

From each patient 10ml of venous blood was collected from the antecubital vein with syringe, blood was transferred to the vacutainers of 4.5ml containing citrate phosphate dextrose and adenine (CPD-A1) as an anticoagulant. The tubes with citrated blood were centrifuged at 1500 rpm for 5 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets. A sterile pipette is used to separate platelet rich plasma (PRP) and was completely performed inside the biosafety cabinet.

In the operation theatre with the patient in supine position, knee was scrubbed and draped with sterile towels. With the patient knee in 45-90 degrees of flexion so that joint is opened for injection through lateral para-patellar approach. Under aseptic conditions, 8ml platelet concentrate was injected into the knee joint with an 18 gauge needle without local anesthetic. After the procedure Robert Jone's compression bandage applied and the knee were immobilized for 10 minutes. For any possible side effects like dizziness, sweating patients were observed for 30 minutes.

Table I: Distribution of patients.

Gender	No.of patients	Percentage
Male	07	23%
Female	23	77%
Total	30	100%

In this study, 30 osteoarthritic knee joints of kellgren Lawrence radiological grade I-07 and grade II-23 of total 30 patients. Out of which 06 patients (20%) selected were males and remaining 24 patients (80%) were females.

Table II: WOMAC Osteoarthritis index scores.

Sl.No.	WOMAC	Baseline	1 week	2 weeks	3 weeks	1 month	3 months
1.	Pain	496	475	415	348	303	164
2.	Stiffness	202	66	149	127	97	69
3.	Physical function	1548	1532	1154	1053	810	519
4.	Mean	748.6	691.0	572.6	509.3	403.3	250.6

SD	707.6	756.4	520.7	483.6	366.9	237.1
P value unpaired t test	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

In this study, the pain scores of the patients have decreased on the day of infiltration to one week, two weeks & three weeks and one month. Their mean scores have been decreased from the day of infiltration to baseline and three months. It means that there is definite decrease in the pain after infiltration, but on seeing the individual pain scores, for 8 cases pain has subsided completely.

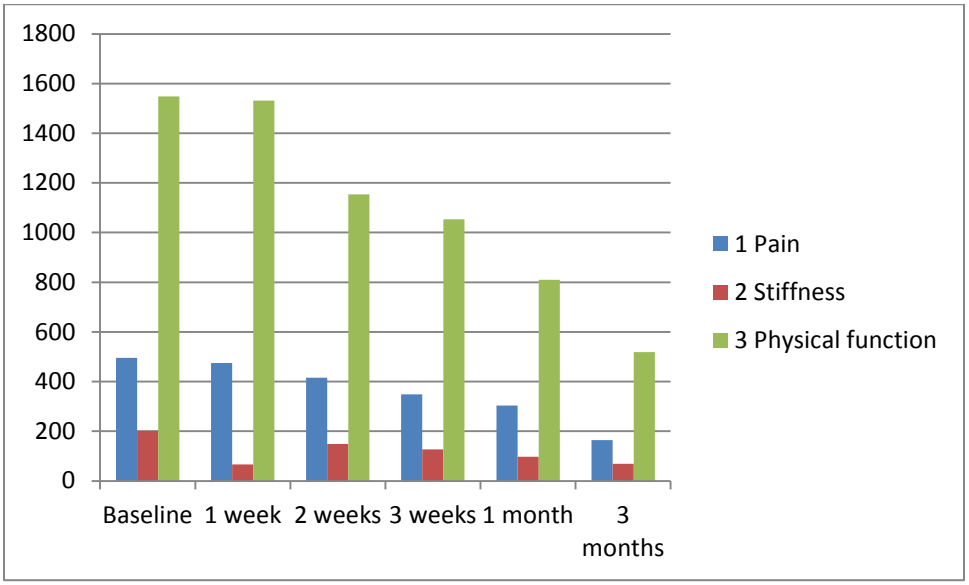

Table III: Visual Analogue scale (VAS) scale scores

Sl.No.	VAS	Baseline	1 week	2 weeks	3 weeks	1 month	3 months
1.	Pain score	120	120	114	88	81	79
2.	NRS	258	199	154	124	87	45
3.	FRS	262	222	176	140	100	50
4.	Mean	213.3	180.3	148.0	117.3	89.3	58.0
	SD	80.8	53.5	31.4	26.6	9.71	18.3
P value unpaired t test		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

In this study, the pain scores, Numerical reading scale and Facial reading scale of the patients have decreased on the day of infiltration to one week, two weeks & three weeks and one month. Their mean scores have been decreased from the day of infiltration to baseline and three months. It means that there is definite decrease in the pain after infiltration, but on seeing the individual pain scores, for 8 cases pain has subsided completely.

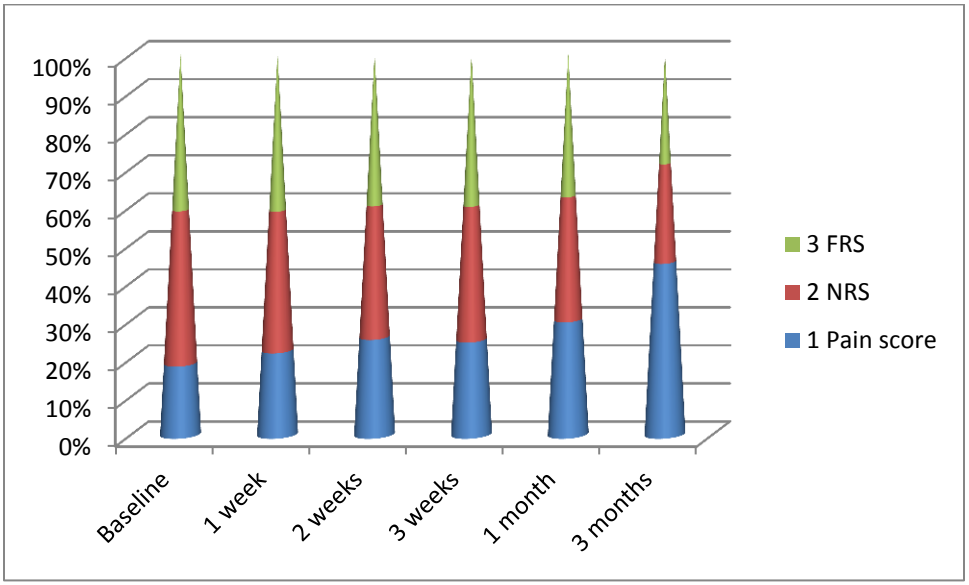

Table: IV Distribution of Osteoarthritis grades according to kellgren Lawrence scale.

Grades	Male	Female
Grade-I	05	13
Grade-II	02	10
Total	07	23

In this study, 30 number of patients were enrolled among them 07 (23%) are male patients and 23(77%) are female patients.

Table: V Distribution of patient's gender

Gender	Grade-I	Grade-II
Male	05	02
Female	13	10
Total	18	12

In this study, females (13 patients) are rapidly prone to osteoarthritis due to lifestyle modifications.

Table: VI Distribution of patient's age

Age category	Gender	
	Male count	Female count
less than 35	00	02
35-44	01	09
45-54	04	08
55-64	02	04
65-74	00	00

Table VII: Effect of platelet rich plasma Vs gender

GENDER	PRP		TOTAL
	Effective	Not-effective	
Male	5(71%)	2(29%)	7(100%)
Female	18(78%)	5(22%)	23(100%)

In the study group, the PRP treatment was effective in 78% females (18cases), 71% males (5 cases) and not effective in 29% males (2 cases), 22% females (5 cases) were observed.

Table VIII: Effect of platelet rich plasma Vs Age

AGE	PRP		TOTAL
	Effective	Not-effective	
Less than 35	02(100%)	00(0%)	02(100%)
35-44	05(71%)	02(29%)	07(100%)
45-54	07(70%)	03(30%)	10(100%)
55-64	02(33%)	04(67%)	06(100%)
65-74	03(60%)	02(40%)	05(100%)

In the study group, the PRP treatment was effective in less than 35 age group (for two patients pain has been subsided completely. And less or not effective in 35-44 age groups.

Table IX: Effect of platelet rich plasma Vs grade

GRADE	PRP		TOTAL
	Effective	Not-effective	
Grade-I	13(72%)	05(28%)	18(100%)
Grade-II	08(67%)	04(33%)	12(100%)

In the study group, the PRP treatment was effective in Grade-I among 18 patients i.e, stiffness score of the patients have decreased on the day of infiltration to one month and three months (stiffness had completely subsided)

DISCUSSION

The effectiveness of PRP in decreasing pain, stiffness and physical function was assessed and scored on WOMAC and VAS with following parameters were studied. The results were analyzed by using unpaired t-test and chi-square test. Age distribution shows that mean age in group-I (effective) to be 2.422 and the mean age in group-II (Not-effective) to be 6.275. The p-value derived using unpaired t-test for group-I is 0.0262 and group-II is 0.0001, rendering age factor insignificant gender distribution were comparable on both groups using 80% being female and 20% being male. The p-value using chi-square test is 0.0026 .The gender factor was significant. The plasma rich protein versus gender the t-statistics shows that effective with 4.95(0.0001) and not-effective with 3.393(0.0026). The gender factor was significant. The plasma rich protein versus grade the t-statistics shows that grade-I with 11.12(<0.0001) and grade-II with 10.71(<0.0001) which is significant thus the study ensured that all patients were comparable on baseline characters (effective and non-effective). The global WOMAC showed a mean of baseline with 748.6(<0.0045)and after three months 250.6(<0.0001) along with WOMAC the VAS scale also used shows a mean of baseline with 213.3(t-statistic 14.2) and after three months the review as follows 58.0(<0.0001) the p-value using unpaired t-test turned significant. The study showed a significant decrease in global WOMAC score and VAS scale, which was also consistent throughout the study period. The individual variables such as pain, stiffness and physical function were assessed mean score for pain showed decreased from baseline of 748.6 to 250.6 at 6 weeks post injection. At the end of three months follow up, mean was 58.0.The p-value using unpaired t-test showed significant improvement. Secondary variable stiffness showed significance difference at 2 months follow up and 3 months follow up the mean of physical function decreased from post injection. Visual analog showed a decrease in mean of 213.3 to 58.0 which denotes a change of patient's perception of pain from intense, dreadful, horrible pain to mild annoying pain in patients. The VAS scale p-value using unpaired t-test shows that the significant improvement in patients.

CONCLUSION

Osteoarthritis represents a failure of diarthrodial joint, characterized by degenerative changes in

articular cartilage of joint. The management of osteoarthritis has undergone sea changes during last century. Osteoarthritis has been managed by conservative methods like lifestyle changes and physiotherapy and surgical methods like total knee replacement (TKR) depending upon the stage of disorder. A constant search for molecule that could aid in cartilage regeneration, thus interfering in disease process has thrown up suprises.one such ideology is garnering the beneficial effect of growth factors in platelets to regenerate cartilage in a synovial joint. Our study depends on injecting a highly concentrated mix of platelets into joint cavity and observing the patients for reduction in symptoms of pain, stiffness and improvement in physical function. Our study has revealed a consistent reduction in pain and stiffness and a clear improvement in lifestyle of the patients. Our study has thrown up an interesting choice of treatment of knee osteoarthritis and it has proved efficacious in the observation period of three months. There were no major complications or incidences of infection in patients. Long term follow up needed with ESR (erythrocyte sedimentation rate) and M.R.I to assess the regeneration of cartilage.

REFERENCES

[1]. Wang, Z., Mudalal, M., Sun, Y. et al. The Effects of Leukocyte-Platelet Rich Fibrin (L-PRF) on Suppression of the Expressions of the Pro-Inflammatory Cytokines, and Proliferation of Schwann Cell, and Neurotrophic Factors. Sci Rep 10, 2020, 2421.

[2]. Patrick A. Smith. Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis. The American Journal of Sports Medicine, Vol. 44, No. 4. 2016

[3]. Chiara Leuratti, Luca Loprete, Matteo Rossini, Valeria Frangione, Stefano Rovati, and Milko Radicioni1. Pharmacokinetics and Safety of a Diclofenac Sodium 75 mg/1 mL Solution (Akis®/Dicloin®) Administered as a Single Intravenous Bolus Injection in Healthy Men and Women. Eur J Drug Metab Pharmacokinet. 44(5), 2019, 681–689.

[4]. Dr Bansilal Karra, Dr.koppula Sreeja, Velicharla Raviteja. Role of Intra Articular Injections of Autologous Platelet Rich Plasma in Osteoarthritis of Knee Joint. International Journal of Medical Science and Clinical Invention, 6(3), 2019.

[5]. Grazyna Stanczuk,1,2 Gwendoline Baxter,1 Heather Currie,3 James Lawrence,1 Kate Cuschieri,4 Allan Wilson,5 Marc Arbyn6. Clinical validation of hrHPV testing on vaginal and urine self samples in primary cervical screening (cross-sectional results from the Papillomavirus Dumfries and Galloway—PaVDaG study). BMJ Open. 6, 2016, e010660.

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